



UNITED STATES PATENT AND TRADEMARK OFFICE

Handwritten signature

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|-------------------------------|------------------------|
| 09/729,653 | 12/04/2000 | Biaoyang Lin | P-IS 4367 | 3087 |
| 41552 7590 06/14/2007 MCDERMOTT, WILL & EMERY 4370 LA JOLLA VILLAGE DRIVE, SUITE 700 SAN DIEGO, CA 92122 | | | EXAMINER DAVIS, MINH TAM B | |
| | | | ART UNIT 1642 | PAPER NUMBER |
| | | | MAIL DATE 06/14/2007 | DELIVERY MODE PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/729,653

Applicant(s)

LIN, BIAOYANG

Examiner

MINH-TAM DAVIS

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04/13/07.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33-65 is/are pending in the application.
- 4a) Of the above claim(s) 33-39 and 50-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 40-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- ☐ Notice of Informal Patent Application
- ☐ Other: _____

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claims 1-32, and adds new claims 33-65.

Since applicant has elected Group II, the polypeptide SEQ ID NO:2, for action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the embodiments of new claims 33-39, 50-65, directed to a method for diagnosis or predicting susceptibility to a prostate neoplastic condition have been withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03. Newly submitted claims 33-39, 50-65 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 33-39, 50-65 are related to the originally presented invention as product and process.

It is noted that the examiner has required restriction between product and process claims (see Restriction requirement of 02/26/02 for detailed reasons of record).

Accordingly, claims 40-49 are examined in the instant application.

Claims 33-39, 50-65 are withdrawn from consideration as being drawn to non-elected invention.

Withdrawn Rejection

The 112, first paragraph, scope rejection of claim 26, and the 102 rejection of claim 26 were withdrawn in view of the cancellation of claim 26.

NEW REJECTIONS DUE TO THE AMENDMENT

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40-49 are indefinite, because claims 40-49 are confusing. It is not clear how an amino acid sequence having only a few amino acids could have 55% or more identity to the full length SEQ ID NO:2.

It is noted that “an” amino acid sequence as cited in claim 40 could be interpreted as a sequence having as little as a few amino acids. A sequence having 55% or more identity to SEQ ID NO:2 as cited in claim 40 is interpreted as a sequence having 55% or more identity to full length SEQ ID NO:2.

This rejection could be obviated by amending claim 40, for example, to replace “an amino acid sequence” with “the amino acid sequence”.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses that the PAMP polypeptide of SEQ ID NO:2 is a predicted polypeptide encoded by SEQ ID NO:1 (p.8, last paragraph and Example I, on pages 62-63), wherein SEQ ID NO: 1 is expressed in a prostate specific manner, in both normal and cancer prostate tissues, and is androgen regulated when tested in prostate carcinoma cell line LNCaP (Examples II and III, on pages 63- 67 and figure 5). In the Declaration by Dr. Biaoyang Lin of 08/27/03, it was shown that SEQ ID NO:2 is overexpressed in prostate cancer tissue as compared to normal prostate tissue. The specification discloses PAMP polypeptides that are similar to human PAMP and having 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more identity to SEQ ID NO:2 (p.19).

The biological function of SEQ ID NO:2 however is not disclosed. Further, there is no disclosure the specification domains of SEQ ID NO:2 that are responsible for the function of SEQ ID NO:2, nor structure of any of PAMP polypeptides that are similar to human PAMP and having 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more identity to SEQ ID NO:2

Art Unit: 1642

The art does not teach SEQ ID NO:2.

Claims 40-49 encompass a **genus of PAMP variant polypeptides** with unknown structure and function, provided they have 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more identity to SEQ ID NO:2.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that “[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials.” Id. At 1567, 43 USPQ2d at 1405. The court also stated that

a generic statement such as “vertebrate insulin cDNA” or “mammalian insulin cDNA” without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that “naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.” Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described.

“A description of a genus of cDNAs may be achieved by means of a recitation of a

representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.” Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that □ the written description requirement can be met by “show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristicsi.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.” Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

In this case, the specification does not describe the PAMP variant polypeptides in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure, other than SEQ ID NO:2, to support the broad breath of the claimed genus. Nor is there any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single polypeptide, SEQ ID NO:2, this does not provide a description of the PAMP variant polypeptides, that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe the PAMP variant polypeptides, by the standards shown in the example in Lilly. The specification describes only a single polypeptide SEQ ID NO:2. Therefore, it necessarily fails to describe a “representative number” of such species. In addition, the specification also does not describe “structural features common to the members of the genus, which features constitute a substantial portion of the genus.”

The specification does not provide an adequate written description of the PAMP variant polypeptides, that is required to practice the claimed invention. Thus, the specification does not meet the 112, first paragraph written description requirement, and one of skill in the art would reasonably conclude that Applicant did not have possession of the claimed PAMP variant polypeptides at the time the invention was made.

Claim Rejections - 35 USC § 112, First Paragraph, Scope

Claims 40-49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated PAMP polypeptide comprising the amino acid sequence SEQ ID NO:2, does not reasonably provide enablement for an isolated PAMP polypeptide comprising an amino acid sequence having 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more identity to SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The disclosure in the specification has been set forth above.

Claims 40-49 encompass a **genus of PAMP variant polypeptides** with unknown structure and function, provided they have 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or more identity to SEQ ID NO:2.

It is unpredictable that the PAMP variant polypeptides would be overexpressed in prostate cancer tissue as compared to the normal control prostate tissue. It is well known in the art that variants of a sequence do not necessarily express at the same level as the corresponding wild type. For example, Schmid S et al, 2001 (J comparative Neurology, 430(2): 160-71), of record, teach that the variants flip/flop of the gene GluR are expressed at higher levels in neurons in the auditory braistem, as compared to the wild type GluR-A and GluR-B, and that neurons in the central nucleus of the inferior collicullus express high levels of GluR-B flip but only low levels of the other receptor subunits. Conner et al, 1996 (Mol Brain Res, 42: 1-17), of record, teach that full length trkB is found the hippocampus in patients with Alzheimer's disease, but not in hippocampi of either normal age-matched individual or patients with Huntington's disease, and that truncated trkB is found in senile plaques in hippocampus and temporal lobe in both patients with Alzheimer's disease and Huntington's disease, but not in normal brains of aged-

matched individuals (page 8, item 3.1.2). Thus, in view of the teaching in the art, one cannot predict that the variants of SEQ ID NO: 89 would overexpress in ovarian cancer tissue as compared to normal control ovarian tissue, and therefore, one would not know how to practice the claimed method, using the claimed genus of variant Marker genes.

Further, Applicants have not shown how to make the claimed numerous polypeptides, such that they have the properties of SEQ ID NO: 2. It is well known in the art that protein chemistry is unpredictable, and that even a single amino acid substitution or what appear to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristics of a protein. Bowie (Science, 1990, 257:1306-1310) teaches that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie further teaches that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306). The sensitivity of proteins to alterations of even a single amino acid in a sequence are exemplified by Burgess et al (J of Cell Bio. 111:2129-2138, 1990), of record, who teach that replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by

Art Unit: 1642

glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein and by Lazar et al (Molecular and Cellular Biology, 1988, 8:1247-1252), or record, who teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution will often dramatically affect the biological activity and characteristics of a protein. As an example, one cannot predict that a sequence taught by Nagase et al, 2001, which is expressed in brain, and which has 64% similarity with SEQ ID NO:2, as shown by MPSRCH sequence similarity search (MPSRCH search result, 2002, us-09-729-653-2.rspt, pages 1-2, of record) would have the property of SEQ ID NO:2, such as overexpression in prostate cancer tissue as compared to normal prostate tissue. Thus, in view of the teaching in the art, one cannot predict that the PAMP variant polypeptides would have properties of SEQ ID NO: 2.

MPEP 2164.03 teaches that “the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is

unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling.”

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1642

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SHANON FOLEY can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
June 07, 2007

Art Unit: 1642

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SHANON FOLEY can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS

June 07, 2007

/Larry R. Helms/

Supervisory Patent Examiner